APPENDIX A
"Clean" Version of Each Paragraph/Section/Claim
37 C.F.R. § 1.121(b)(ii) and (c)(i)

SPECIFICATION:

Replacement for the paragraph beginning at page 3, line 11:

A2 The present invention also provides a liquid pharmaceutical composition comprising about 2,200 MRC units of salmon calcitonin, about 10 mM citric acid, about 0.2% phenylethyl alcohol, about 0.5% benzyl alcohol, and about 0.1% TWEEN® 80.

Replacement for the paragraph beginning at page 3, line 16:

A2 The present invention further provides a liquid pharmaceutical composition comprising about 2,200 MRC units of salmon calcitonin, about 20 mM citric acid, about 0.2% phenylethyl alcohol, about 0.5% benzyl alcohol, and about 0.1% TWEEN® 80.

Replacement for the paragraph beginning at page 12, line 24:

A3 Example 1

The following study examines the effect of the concentration of citric acid on the bioavailability and plasma concentration of nasally administered salmon calcitonin. Rats were administered intranasally as described previously 20µl of rsCT (200µg/ml) in 0.85% sodium chloride, 0.1% TWEEN® 80, 0.2% phenylethyl alcohol, 0.5% benzyl alcohol and varying amounts of citric acid adjusted to pH 3.7 at t=0, 20, 60 and 90 minutes. Samples of blood were taken prior to the administration of rsCT at these time points as well as at t=120 and 150 minutes. The resulting plasma samples were analyzed for rsCT by radioimmunoassay. Maximum rsCT levels were detected at t=120 minutes. The results of this study as shown in Table 1 indicate that the bioavailability and peak concentration of rsCT was a function of the concentration of citric acid in the formulation.

Replacement for the paragraph beginning at page 14, line 12:

A4 Example 2

The following study examines the effect of different preservatives on the plasma concentration of nasally administered salmon calcitonin. Rats were administered intranasally as described previously 20µl of sCT (200µg/ml) in 0.85% sodium chloride, 0.1% TWEEN® 80 and

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A4 a combination preservatives of either 0.2% phenylethyl alcohol and 0.5% benzyl alcohol or 0.27% methyl parabens and 0.04% propyl parabens at t=0, 30, 60 and 90 minutes. The results of this study as shown in Table 2 indicate that the bioavailability and peak concentration of rsCT are not significantly affected by the addition of the different preservatives.

Replacement for the paragraph beginning at page 15, line 11:

A5 Example 3

The following study examines the effect of the concentration of citric acid on the stability of salmon calcitonin stored for varying periods at a temperature of 50°C. Nasal formulations containing sCT (200μg/ml), 0.25% phenylethyl alcohol, 0.5% benzyl alcohol and 0.1% TWEEN® 80 were adjusted to pH 3.7 with either HCl or the indicated amount of buffered citric acid. The formulations were stored at 50°C in sealed glass containers for the indicated amount of time and analyzed for sCT by high performance liquid chromatography. The results as shown in Table 3 indicate that in the absence of citric acid, the amount sCT in the formulation decreased steadily between 0 and 9 days after the study was begun. In the presence of citric acid (10-50 mM) the rate of disappearance of sCT decreased significantly. However, as the concentration of citric acid was further increased, the rate of sCT disappearance from vials stored at 50°C increased in proportion to the amount of buffered citric acid in the formulation.

CLAIMS:

A6 (Amended) 16. The liquid pharmaceutical composition of claim 1 further containing at least 0.1% by weight of polyoxyethylene(20) sorbitan monooleate.

A7 B (Amended) 18. A liquid pharmaceutical composition comprising about 2,200 MRC units of salmon calcitonin, ~~about~~ 10 mM citric acid, about 0.2% phenylethyl alcohol, about 0.5% benzyl alcohol, and about 0.1% polyoxyethylene(20) sorbitan monooleate.

(Amended) 19. A liquid pharmaceutical composition comprising about 2,200 MIC units of salmon calcitonin, about 20 mM citric acid, about 0.2% phenylethyl alcohol, about 0.5% benzyl alcohol, and about 0.1% polyoxyethylene(20) sorbitan monooleate.